

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 96/12897

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C12N15/19 C07K14/47 C07K14/52 C12N5/10
A61K38/17 C07K16/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	THE JOURNAL OF IMMUNOLOGY, vol. 154, no. 7, 1 April 1995, pages 3333-3340, XP002032346 MIYAKE ET AL.: "RP105, a novel B cell surface molecule implicated in B cell activation, is a member of the Leucine-rich repeat protein family" see abstract see page 3336; figure 2 see page 3337, left-hand column, paragraph 2 see page 3338; figure 4 --- -/--	11-19

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *&* document member of the same patent family

Date of the actual completion of the international search

5 June 1997

Date of mailing of the international search report

13. 06. 97

Name and mailing address of the ISA

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09/870, 997 #7

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/12897

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>DATABASE EMBL ENTRY MM04637 Accession Number W67046, 15 June 1996 MARRA ET AL.: "The WashU-HHMI mouse EST project" XP002032347 see abstract & Unpublished</p>	21-29
P,X	<p>--- DATABASE EMBL ENTRY MM3831 Accession Number W08383, 27 April 1996 MARRA ET AL.: "The WashU-HHMI mouse EST project" XP002032348 see abstract & Unpublished</p>	21-29
P,X	<p>--- -DATABASE EMBL ENTRY MM93010 Accession Number W17930, 4 May 1996 MARRA ET AL.: "The WashU-HHMI mouse EST project" XP002032349 see abstract & Unpublished</p>	21-29
P,X	<p>--- DATABASE EMBL ENTRY MM1705 Accession number W11170, 29 April 1996 MARRA ET AL.: "The WashU-HHMI mouse EST project" XP002032350 see abstract & Unpublished</p>	21-24
P,X	<p>--- DATABASE EMBL ENTRY HS309B01B Accession number D62634, 29 August 1995 FUJIWARA ET AL.: XP002032351 see abstract & Unpublished</p>	41-44
E	<p>--- WO 97 04097 A (GENETICS INST) 6 February 1997 Seq.ID:1/2 see page 33 - page 34 see page 39 - page 42; claims</p>	51-60
2 A	<p>--- WO 95 18826 A (SCHERING CORP ;INST NAT SANTE RECH MED (FR)) 13 July 1995 see page 50 - page 63 ---</p>	51-60

-/--

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207
10/2/200

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 96/12897

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 914 025 A (MANOIL COLIN ET AL) 3 April 1990 see the whole document ---	1-10
A	JOURNAL OF BACTERIOLOGY, vol. 177, no. 1, 1 January 1995, pages 59-65, XP000560419 ENG MONG LIM ET AL: "IDENTIFICATION OF MYCOBACTERIUM TUBERCULOSIS DNA SEQUENCES ENCODING EXPORTED PROTEINS BY USING PHOA GENE FUSIONS" ---	
A	JOURNAL OF CELLULAR BIOCHEMISTRY, vol. 21A, 10 March 1995 - 4 April 1995, page 19 XP002027246 JACOBS ET AL.: "A novel method for isolating eukaryotic cDNA clones encoding secreted proteins" ---	
T	US 5 536 637 A (JACOBS KENNETH) 16 July 1996 -----	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 96/12897

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 10, 20, 30, 40, 50, 60
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although these claims are directed to a method of treatment of (diagnostic method practised on) the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

5 inventions * see continuation-sheet PCT/ISA/210 *

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

1) claims 1-10 totally.

Nucleotide sequence as in Seq.ID:1 encoding polypeptide as in Seq.ID:2, fragments, compositions and potential therapeutical uses.

2) claims 11-20 totally.

Nucleotide sequence as in Seq.ID:3 encoding polypeptide as in Seq.ID:4, fragments, compositions and potential therapeutical uses.

3) claims 21-30 totally.

Nucleotide sequence as in Seq.ID:5 encoding polypeptide as in Seq.ID:6, fragments, compositions and potential therapeutical uses.

4) claims 31-50 totally.

Nucleotide sequence as in Seq.ID:7/9 encoding polypeptide as in Seq.ID:8/10, fragments, compositions and potential therapeutical uses.

5) claims 51-60 totally.

Nucleotide sequence as in Seq.ID:11 encoding polypeptide as in Seq.ID:12, fragments, compositions and potential therapeutical uses.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 96/12897

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9704097 A	06-02-97	AU 6712396 A AU 6768596 A WO 9707198 A	18-02-97 12-03-97 27-02-97
WO 9518826 A	13-07-95	AU 1520895 A EP 0733069 A JP 9501572 T	01-08-95 25-09-96 18-02-97
US 4914025 A	03-04-90	NONE	
US 5536637 A	16-07-96	NONE	

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
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Intellectual Property Dep't
24 rue Royale
F-75008 Paris
FRANCE

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

REÇU 2 - AVR. 2001

Applicant's or agent's file reference 78.W01		Date of mailing (day/month/year) 29/03/2001
International application No. PCT/IB 00/ 01938		International filing date (day/month/year) 07/12/2000
Applicant GENSET et al.		


- This International Searching Authority
 - considers that there are 241 (number of) inventions claimed in the international application covered by the claims indicated ~~on~~ on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~on~~ on the extra sheet:
 - ☒ has carried out a partial international search (see Annex) ☐ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:
1-26 (all partially)
 - will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid
- The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:

<u>EUR 945,00</u>	x	<u>240</u>	=	<u>EUR 226.800,00</u>
Fee per additional invention		number of additional inventions		total amount of additional fees

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.
- ☐ Claim(s) Nos. _____ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority
 European Patent Office, P.B. 5818 Patentlaan 2
 NL-2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer
Heike Zoglauer

This International Searching Authority found multiple (groups of) inventions in this application, as follows:

Invention 1: Claims: 1-26 (all partially)

Isolated polynucleotides, polypeptides, expression vectors, host cells, non-human transgenic animals methods and antibodies relating to the nucleotide sequence of SEQ ID No:1 and the amino acid sequence of SEQ ID No:242

Inventions 2 to 241: Claims: 1-26 (all partially)

Idem as invention 1, but relating to each of the nucleotide sequences of SEQ ID Nos:2 to 241 and the corresponding amino sequences of SEQ ID Nos:243 to 482, where invention 2 is limited to SEQ ID Nos:2 and 243, invention 3 is limited to SEQ ID Nos:3 and 244,....., and invention 241 is limited to SEQ ID Nos:241 and 482.

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

The present application discloses the cloning of 241 human genes encoding secreted proteins. Human genes encoding secreted proteins are however known from the prior art. For example, WO 97/07198 discloses polynucleotides encoding secreted human and murine proteins and their potential application in therapy. "Science 1993 261:600-603" and "Gene 1997 198:289-296" disclose methods of screening for murine and human cDNAs respectively, encoding human mammalian proteins. "Nucleic Acids Res. 1986 14(11): 4683-4690" discloses a method to identify secretory signal sequences, and to predict the site of cleavage between the signal peptide and the mature protein.

In light of this prior art, the problem underlying the present application is the provision of further cDNAs, encoding human secreted proteins and the corresponding polypeptides. The solutions as disclosed and claimed in the current application can be summarised as the provision of 241 DNA sequences (SEQ ID Nos:1-241) and the corresponding polypeptides (SEQ ID Nos:242-482).

Due to the fact that polynucleotides encoding mammalian secreted proteins were already known from the prior art, due to the existence of corresponding methods of screening, due to the essential differences between the primary structures of the sequences claimed, and due to the fact that no other technical feature can be distinguished which, in light of the prior art could be regarded as special, common technical feature, the ISA is of the opinion that there is no single inventive concept underlying the plurality of different inventions of the present

INVITATION TO PAY ADDITIONAL FEES

International application No.

PCT/IB 00/01938

application in the sense of Rule 13.2 PCT.

Consequently there is a lack of unity and the different inventions not belonging to a common inventive concept are formulated as the different subjects on the communication pursuant to Article 17(3)(a) PCT.

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
- see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.
3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.
4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>DATABASE GENESEQ [Online] AC No. Y76144, 23 March 2000 (2000-03-23) RUBEN SM ET AL: "Human secreted protein encoded by gene 21" XP002163702 polypeptide 100% identical with SEQ ID No:242 over its entire length (508 aa) abstract</p>	1-26
P,X	<p>--- DATABASE GENESEQ [Online] AC No. Z65270, 23 March 2000 (2000-03-23) RUBEN SM ET AL: "Human secreted protein gene 21" XP002163703 Polynucleotide with 99.9% identity to SEQ ID No:1 over 2138 nucleotides abstract</p>	1-26
X	<p>--- DATABASE EMBL [Online] AC No. AI911546, 30 July 1999 (1999-07-30) NATL. CANCER INST.: "ty73d05.x1 NCI CGAP Kid11 Homo sapiens cDNA clone IMAGE:2284713" XP002163704 Polynucleotide 100% identical with SEQ ID No:1 over 519 nucleotides abstract</p> <p align="center">---</p> <p align="center">-/--</p>	1-10, 15-17

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL [Online] AC No. AI361251, 7 January 1999 (1999-01-07) NATL. CANCER INST.: "qy42e02.x1 NCI CGAP Brn23 Homo sapiens cDNA clone IMAGE:20I4682" XP002163705 Polynucleotide 100% identical to SEQ ID No:1 over 454 nucleotides abstract</p>	<p>1-10, 15-17</p>
A	<p>--- WO 97 07198 A (GENETICS INST) 27 February 1997 (1997-02-27) the whole document</p>	<p>1-26</p>
A	<p>--- JACOBS K A ET AL: "A GENETIC SELECTION FOR ISOLATING CDNAS ENCODING SECRETED PROTEINS" GENE,NL,ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, vol. 198, 1 October 1987 (1987-10-01), pages 289-296, XP002045919 ISSN: 0378-1119 the whole document</p>	<p>1-26</p>
A	<p>--- TASHIRO K ET AL: "SIGNAL SEQUENCE TRAP: A CLONING STRATEGY FOR SECRETED PROTEINS AND TYPE I MEMBRANE PROTEINS" SCIENCE,US,AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, vol. 261, 30 July 1993 (1993-07-30), pages 600-603, XP000673204 ISSN: 0036-8075 the whole document -----</p>	<p>1-26</p>

Patent Family Annex
Information on patent family members

International Application No

PCT/IB 00/01938

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9707198 A	27-02-1997	US 5707829 A	13-01-1998
		AU 727480 B	14-12-2000
		AU 6712396 A	18-02-1997
		AU 727489 B	14-12-2000
		AU 6768596 A	12-03-1997
		CA 2227220 A	06-02-1997
		CA 2229208 A	27-02-1997
		EP 0839196 A	06-05-1998
		EP 0851875 A	08-07-1998
		JP 11510045 T	07-09-1999
		US 6043344 A	28-03-2000
		WO 9704097 A	06-02-1997
		US 6074849 A	13-06-2000
		US 5969093 A	19-10-1999